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Expression and Clinical Significance of Notch Signaling Genes in Colorectal Cancer

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Background: Notch signaling is important in regulating stem cell proliferation and differentiation, as well as in organ and tissue renewal. Increased cell proliferation due to abnormal Notch signaling can also lead to tumor transformation. Notch signaling genes are known to be upregulated in colorectal cancer, indicating that these genes function as tumor suppressors during colorectal tumorigenesis. Currently, a definitive explanation for the function of Notch signaling genes in colorectal cancer is unknown. Specifically, it is unclear whether the expression levels of Notch signaling genes are related to colorectal cancer proliferation and prognosis. This study aims to explore the expression and clinical significance of Notch signaling genes in colorectal cancer.

Methods: Colorectal cancer samples were prospectively collected from patients post-surgery at the 3rd Affiliated Hospital, Nanjing University of Traditional Chinese Medicine. Immunohistochemistry (IHC) of tissue arrays was used to analyze the samples and genes involved in the Notch signaling pathway.

Results: A total of 146 colorectal cancer samples was collected, including samples from 84 men (57.7%) and 62 women (42.5%). The average age of the sample population was 60.8 ± 10.5 years. Notch1 and Notch2 gene expression correlate with tumor pathology type and degree of differentiation, and JAG1 (Jagged 1) and HES1 (hairy-enhancer-of-split 1) gene expression correlate with degree of tumor differentiation. DLL1 (Delta-like 1) gene expression varies significantly with tumor location, and a significant difference was not detected between gene expression and MSI (Microsatellite Instability). Of the 138 patients, 134 (91.8%) participated in the on-site visits, and the average site visit time was 42.3±13.3 months. During this period, 86 patients (71.6%) were tumor-free. After 1 year post-surgery, 93% of patients survived, 74% patients lived for 3 years and 67% patients lived for 5 years. The log-rank test was used to perform univariate analysis, and the COX proportional hazards model was used to perform multivariate analysis. Based on these analyses, tumor prognosis correlates with TNM stage, pathologic type, microsatellite status and Notch2 and JAG1 gene expression. Patients expressing high levels of Notch2 and JAG1 presented with significantly better prognosis relative to patients expressing negative or weak levels of Notch2 and JAG1.

Conclusion: Expression levels of genes associated with the Notch signaling pathway correlate with tumor pathology and degree of differentiation. Notch2 and JAG1 expression levels correlate with survival rate, as determined; however, the underlying mechanism for these correlations remains unclear.